from the group consisting of SEQ ID NOS: 2-10 which differ from the corresponding one or more bases in SEQ ID NO: 1 when the sequences are maximally aligned.

16. (Thrice Amended) The sequence-specific polynucleotide of claim 11 that hybridizes under stringent hybridization conditions to at least 100 contiguous bases of a mycobacterial rpoB sequence selected from the group consisting of SEQ ID NOS: 2-10 or its complement without hybridizing to the M. tuberculosis sequence of SEQ ID NO: 1 or its complement.

Please add the following new claim:

--21. (new) An isolated nucleic acid molecule comprising SEQ ID NO: 7.--

REMARKS

The Office Action mailed October 4, 2001 has been carefully reviewed and the following remarks are made in response thereto.

In view of the foregoing amendment and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

The amendments to claims 1, 2 and 16 are supported, for example, in the specification at page 4, lines 15-34. The amendment to claim 3 is a clarification and is supported by original claim 3. Support for the amendment to claim 11 is found on page 7, lines 15-17. New claim 21 is supported, for example, by original claim 1 and in the specification at page 12, lines 13-30. Applicants respectfully submit that no prohibited new matter has been introduced by the amendment.

I. Summary of the Office Action

1. The Office Action called for the cancellation of non-elected claims 17-20 in response to the final Office Action.

2. The Office Action required the submission of formal drawings within the period of reply set for the Office Action.

3. The Office Action objected to the specification for the recitation of a URL at page 8, line 18.

4. The Office Action rejected claim 3 under 35 U.S.C. §112, 1st paragraph, alleging that the inventors did not have possession of the claimed invention.

5. The Office Action rejected claims 1 & 2 under 35 U.S.C. §112, 1st paragraph for lacking support for the recitation of 300 base pairs.

6. The Office Action rejected claim 3 under 35 U.S.C. §112, 2nd paragraph for being indefinite in the recitation of "perfectly complementary."

7. The Office Action rejected claims 11-16 under 35 U.S.C. §112, 2nd paragraph for being indefinite in the recitation of "stringent conditions."

8. The Office Action indicated the allowability of claims 4-10.

II. Response to the Office Action

At the outset, Applicants note with appreciation the Examiner's indication of allowability of claims 4-10 and his determination that claims 1-3 and 11-16 are free of the prior art.

Formal Drawings Requirement

The formal drawings, prepared in accordance within the guidelines of the objections made of record on form PTO-948, mailed January 29, 2001, are attached hereto.

Election/Restriction

The Final Office Action has required the cancellation of non-elected claims 17-20. In order to be fully responsive to the Office Action, Applicants have canceled the claims without prejudice. Applicants wish to note that they do not surrender or disclaim the right to pursue the subject matter of the canceled claims in another application.

Objection to the specification

The Office Action objected to the specification for containing a URL at line 18 of page 8. The specification has been amended to inactivate the URL, changing the recitation to read simply as an internet location which will not be recognized as a link when the specification is in electronic form. Accordingly, Applicants respectfully request withdrawal of the ground of objection.

Rejection of claim 3 under 35 U.S.C. §112, 1st paragraph as lacking sufficient written description and under 35 U.S.C. §112, 2nd paragraph for being indefinite

The Office Action contends that the specification does not provide support for the claim directed to complementary sequences, alleging that the term "fully complementary" includes in scope sequences which are much larger than the recited sequences of SEQ ID NOs: 2-10. Applicants respectfully traverse this ground of rejection as applied to claim 3 as amended. It is respectfully submitted that it is well understood and accepted in the art that the term "complement" denotes the exact antisense sequence of a recited sequence, base-for-base, not a larger sequence containing the recited sequence. Therefore, the complement of a 700 nucleotide sequence would also be 700 nucleotides. In order to more positively convey this meaning, claim 3 has been amended to recite a "probe which is the complement of a rpoB sequence." Accordingly, Applicants respectfully request withdrawal of the ground of rejection.

Rejection of claims 1 and 2 under 35 U.S.C. §112, 1st paragraph for the recitation of "300" bases

The Office Action contends that the recitation of "300" contiguous bases in claim 1 is not supported in the specification. Claim 1 has been amended to recite that the isolated nucleic acid molecule comprise at least 100 contiguous bases of a sequence selected from the group consisting of SEQ ID NOs: 2, 3, 4, 5, 6, 8, 9 and 10. Applicants note that the De Beenhouwer *et al.* reference cited in a previous Office Action does not disclose segments of any these sequences which are as long as the 100 contiguous bases currently claimed. New claim 21 recites that the isolated nucleic acid molecule must comprise the full length of SEQ ID NO: 7, which is longer than the 267 base sequence internal overlap taught by De Beenhouwer *et al.* Accordingly, Applicants respectfully request withdrawal of the ground of rejection.

Rejection of claim 11-16 under 35 U.S.C. §112, 2nd paragraph for being indefinite

The Office Action contends that the claims are indefinite in the recitation of "stringent conditions" in claim 11 because it is unclear what conditions would qualify as stringent. The Office Action asserts that an example of stringent conditions in the specification does not

fully define the term. The claim has been amended to positively recite the stringency requirement of the hybridization conditions. Following this amendment, there can be no doubt regarding the metes and bounds of the claims, as the stringency conditions are clearly set forth in the claim. Accordingly, Applicants respectfully request withdrawal of the ground of rejection.

Conclusion

In view of the foregoing amendments and remarks, the Applicants respectfully request withdrawal of all outstanding rejections and early notice of allowance to that effect.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

If the Examiner finds that a telephone conference would further prosecution of this application, the Examiner is encouraged to call the undersigned.

Respectfully submitted,
MORGAN, LEWIS & BOCKIUS LLP

Date: April 4, 2002 By: _____
Michael S. Tuscan, Ph.D.
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APPENDIX

Marked-Up Copy of Amendments to Specification and Claims

Added Text

[~~Deleted Text~~]

IN THE SPECIFICATION:

Please replace the paragraph beginning at page 8, line 12 and ending at page 9, line 11 with the following:

-- One example of algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul *et al., J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information ([~~http://~~]www.ncbi.nlm.nih.gov[/]). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al., supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, a cutoff of 100, M=5, N=-4, and a comparison of both strands. For amino acid sequences, the BLAST P program uses as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff (1989) Proc. Natl. Acad. Sci. USA 89:10915).--

IN THE CLAIMS:

1. (Four times amended) An isolated nucleic acid molecule comprising at least 100 [300] contiguous bases from a [an] rpoB sequence selected from the group consisting of SEQ ID NOS: 2, 3, 4, 5, 6, 8, 9 and 10 [2-10].

2. (Four times amended) The isolated nucleic acid molecule of claim 1 comprising a rpoB sequence selected from the group consisting of SEQ ID NOS: 2, 3, 4, 5, 6, 8, 9 and 10 [2-10].

3. (Four times amended) A probe [perfectly complementary to] which is the complement of a [rhoP] rpoB sequence selected from the group consisting of SEQ ID NOS: 2-10.

7. (Thrice Amended) A method of classifying a mycobacteria, comprising

providing a sample comprising a mycobacterial rpoB target nucleic acid;

determining the identity of one or more bases in the target sequence at one or more positions corresponding to one or more bases in a sequence selected from the group consisting of SEQ ID NOS: 2-10 ~~[when the sequences are maximally aligned]~~, wherein the one or more bases of the sequence selected from the group consisting of SEQ ID NOS. 2-10 differ from the corresponding one or more bases in SEQ ID NO. 1 when the sequences are maximally aligned, the identity of the one or more bases characterizing the species of mycobacteria that is present in the sample; comparing the identified one or more bases in the target sequence to at least one sequence selected from the group consisting of SEQ ID NOS: 2-10; and

classifying the mycobacteria from the extent of similarity between the one or more bases identified in the target sequence and the corresponding one or more bases in the compared sequences.

9. ~~[(Thrice]~~**(Four times** Amended) The method of claim 8, wherein the identity of at least 20 bases in the target sequence at positions corresponding to the one or more bases in the sequence selected from the group consisting of SEQ ID NOS: 2-10 ~~[are identified]~~ is determined.

10. ~~[(Thrice]~~**(Four times** Amended) The method of claim 9, further comprising comparing the at least 20 determined bases with at least 20 bases occupying corresponding positions in each of at least nine sequences selected from the group consisting of SEQ ID NOS: 2-10.

11. (Four times amended) A sequence-specific polynucleotide probe or primer that hybridizes under stringent hybridization conditions to at least a segment of a mycobacterial rpoB sequence selected from the group consisting of SEQ ID NOS: 2-10 or its complement without hybridizing to the [M. tuberculosis] *M. tuberculosis* sequence of SEQ ID NO: 1 or its complement, wherein the segment includes at least 20 bases of a sequence selected from the group consisting of SEQ ID NOS[-]: 2-10 which differ from the corresponding bases in SEQ ID NO: 1 when the sequences are maximally aligned; wherein said stringent hybridization conditions comprise 5 x SSPE and a temperature of 25-30°C.

16. ~~[(Twice]~~**(Thrice** Amended) The sequence-specific polynucleotide of claim 11 that hybridizes under stringent hybridization conditions to at least ~~[300]~~ 100 contiguous bases of a mycobacterial rpoB sequence selected from the group consisting of SEQ ID NOS: 2-10 or its complement without hybridizing to the M. tuberculosis sequence of SEQ ID NO~~[.]~~**:** 1 or its complement.